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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/763,377	01/23/2004	Yat Sun Or	ENP-074 (4014.1074 US)	7571

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	
MAIL DATE	DELIVERY MODE
11/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,377	OR, YAT SUN	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 10/22/2008 has been entered.

The Request for Continued Examination filed 10/22/2008 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 13-15 have been canceled.

2. New Claim 16 has been added.

3. Claim 1 has been amended.

4. Remarks drawn to rejections under 35 USC 112, first paragraph and 103(a)

Claims 1-12 and 16 are pending in the case.

The rejection of Claim 1 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the process as instantly claimed using macrolide antibiotic, does not reasonably provide enablement for a process using any macrocyclic compound, maintained in the Final Rejection of 12/15/2006 has been withdrawn in view of The Board's Decision rendered 8/25/2008.

The rejection of Claim 15 under 35 U.S.C. 102(b) as being anticipated by Or et al (WO 99/21864), maintained in the Final Rejection has been rendered moot by cancellation of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Or et al (WO 99/21864), of record.

Or et al teaches a process for making a bridged macrocyclic compound (formula 14, page 36) comprising the reaction of the macrocyclic compound of formula 1 (page 34, has at least two nucleophilic groups) with the bridging components H_2N-$(CH_2)_m$-A-B-D-X and $(CH_2)_2$-C=CH_2 (the second bridging component with the double bond forms a pi-allyl complex with a metal; page 36, scheme 3) to yield the bridged product. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic. The macrocyclic compound of Or (formula 1, page 34) has two sugar units attached to it. The macrocyclic compound of Or has an ethyl group attached to the carbon adjacent to the ring oxygen. This is the group L in structure I in instant claim 6. It also

has a second carbonyl group (at the top left of formula 1, page 34), which corresponds to X and Y in instant claim 5 taken together to form a carbonyl group.

However, Or et al teach the use of two separate bridging components to form the bridged product instead of a single bifunctional bridging component as instantly claimed. But the two individual bridging components have a functional group on one end through which the attachment to the macrocyclic compound is achieved. One of them also has a double bond, which can form a pi-allyl metal complex (as recited in instant claim 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the process of Or to make a bridged macrocyclic product as instantly claimed using a single bifunctional bridging component as instantly claimed since the starting material, the bridging components similar to one instantly claimed and the process steps as instantly claimed is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to use the process of the prior art for making a bridged macrocyclic compound using a single bifunctional bridging component since the use of a single bridging bifunctional component would achieve the said bridging in two steps compared to three steps that the process of Or requires. One of ordinary skill in the art would be motivated to extend this to other macrocyclic compounds in order to develop new derivatives having improved antibacterial activity since there is a continuing need to identify new derivatives which may have less potential for developing resistance (Or, page 1, lines 15-20). One of ordinary skill in the art would also recognize that the process of making the bridged macrocyclic compound could be extended with a reasonable expectation of success to other

derivatives of erythromycins since all of them have the same core structure and the required nucleophilic moieties.

Response to Applicants' Arguments

Applicants have traversed the 103(a) rejection of record arguing that:

1. Claim 1 has been amended to recite that both nucleophilic moieties react with the bridging component. In the method of Or two reactive groups on the macrocycle react with two different components, not a single component as instantly claimed.

2. In the process of Or one of the macrocyclic functional groups that reacts with the bridging component is not nucleophilic. The imidazole carboxylic ester moiety, which reacts with the primary amine component H_2N-$(CH)_m$-A-B-D-X is electrophilic (as supported by Boufi et al, Langmuir, 2008, 24, 7309-7315). This is in contrast to the instant process wherein two nucleophilic groups on the macrocycle react with the bridging component.

3. There is no teaching or suggestion by Or of an alternative process for bridging.

Applicants' arguments are not found to be persuasive.

Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988 and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Or et al teaches a process for making a bridged macrocyclic compound (formula 14, page 36) comprising the reaction of the macrocyclic compound of formula 1 (page 34) with the

bridging components H_2N-$(CH_2)_m$-A-B-D-X and $(CH_2)_2$-C=CH_2 (the second bridging component with the double bond forms a pi-allyl complex with a metal; page 36, scheme 3) to yield the bridged product. The macrocyclic compound of Or is a derivative of erythromycin and is an antibiotic and is structurally very close to the macrocyclic compound used for the said bridging in the instant process. The macrocyclic compound and the bridging components, which have nucleophilic moieties and a double bond capable of forming a pi-allyl metal complex, disclosed by Or also meet the limitations of the instant claims. The instant claims are not drawn to a specific type of bridged compound that is distinct from that disclosed in the prior art.

The prior art process involves attaching two individual components, both of which meet the limitations of the instant claims, to the macrocycle and then coupling the two together to form the bridge. One of skill in the art will recognize that the same type of bridging can be achieved by having all the structural limitations of the bridging group in a single component, i.e. having the bridging group bifunctional and also having a double bond that can form a complex with a metal.

It is true that in Or's method that the imidazole carboxylic ester moiety, which reacts with the primary amine component H_2N-$(CH)_m$-A-B-D-X is electrophilic. In Scheme 1 (page 34) the allylic bridging component is attached to the macrocycle via the reaction of a nucleophilic moiety (hydroxyl at the C-6 position) on the macrocycle with allyl bromide (page 34, Scheme 1, conversion of compound 3 to compound 4, wherein R is –$(CH)_2$-$CH=CH_2$). This same reaction can also be done for attaching the bridging component on the other side of the macrocycle. Doing this will eliminate the steps of having to make a carbonyl imidazole ester and then

reacting that with the other end of the bridging component and hence reduce the number of steps needed.

It is well within the purview of one of skill in the art to recognize all of this from the teachings of the prior art. The prior art need not explicitly teach this. So, making the compound as instantly claimed is an obvious variant and can be recognized and performed based on the choice of experimental design. Hence, to choose a method of achieving the bridging step similar to the one disclosed in the prior art (the end result being the same-bridging) by recognizing the alternative method that is within the skill level of the artisan is not seen as erroneous. The alternative method also need not be taught or suggested by the prior art.

The formation of a bridge using a bridging component that has the structural limitations in a single component would be expected by the skilled artisan to give the same good yield as reported in the prior art using two individual components, if not higher. There is a reasonable expectation of success. Hence, the process of Or as disclosed in WO '084 is similar to the one instantly claimed and achieves the same end result as instantly claimed and does render the instant claims obvious. The fact that bridging can be achieved in fewer steps compared to that of Or can be recognized by one of ordinary skill in the art and is also the motivation for carrying out the process as instantly claimed.

Conclusion

Claims 1-12 and 16 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ganapathy Krishnan/

Examiner, Art Unit 1623

/Shaojia Anna Jiang/

Supervisory Patent Examiner, Art Unit 1623